

REMARKS

Claims 1, 2, 4-20, 22-49, 51-60, and 62-72 are pending in the present patent application. Applicants respectfully note that the Office Action does not make any reference to claims 65 and 66 which should be pending in this application. Claim 72 is amended to depend from claim 71 in accordance with the Examiner's suggestion in paragraph 1 of the Office Action. Applicants respectfully request that the amendment of claim 72 be entered as this prepares the claim for allowance or places the application in better form for appeal.

Applicants thank Examiner Cole for indicating that claims 1, 2, 4-20, 22-49, and 51-59 are allowed. Therefore, there are only two outstanding issues with respect to this application. First, the Office Action objects to claim 72 and suggests that this claim be amended to depend from claim 71. Second, the Office Action rejects claims 60, 62-64, and 67-72 under the first paragraph of 35 U.S.C. § 112 alleging that these claims fail to comply with the enablement requirement. No other rejections or objections remain in this application.

Applicants respectfully request that the Examiner consider the following remarks with respect to the rejection set forth in the Office Action. In view of the following remarks, reconsideration and withdrawal of the objections and rejections to the claims in the application is respectfully requested. Applicants believe that the application is now in condition for allowance.

Objection to Claim 72

The Office Action objects to claim 72 indicating that this claim should depend from claim 71. Applicants have amended claim 72 to depend from claim 71 as recommended in the Office Action. Therefore, Applicants respectfully contend that this objection has been addressed and request that the objection be withdrawn.

**Rejection of Claims 60, 62-64, and 67-72
Under the First Paragraph of 35 U.S.C. § 112**

The Office Action rejects each of claims 60, 62-64, and 67-72 under the first paragraph of 35 U.S.C. § 112 alleging that the specification fails to enable these claims. With respect to this rejection, the Office Action states,

Claims 60, 62-64, and 67-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for metallized layer, self-assembled monolayer then metal salts with liquid crystal on top, does not reasonably provide enablement for functional groups with metal complexes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

For the reasons set forth below, Applicants respectfully traverse the rejection of claims 60, 62-64, and 67-72 for allegedly failing to comply with the enablement requirement.

As set forth in the above paragraph, the Office Action finds that the specification enables the metallized layer, the self-assembled monolayer, the self-assembled monolayer with metal salts, and the application of the liquid crystal layer. However, the Office Action concludes that the specification is not enabling for functional groups with metal complexes. Applicants believe that this conclusion is based on an incorrect understanding of these terms in the claims.

Independent claim 60 is set forth below for the Examiner's convenience.

60. (Previously Presented) A device for detecting the presence of a compound in a sample, comprising:

(a) a surface including functional groups, wherein the functional groups are bonded to a metal forming a metal complex, wherein the metal is selected from the group consisting of Cd, Rb, K, Li, Cs, Ag, Au, Zn, Ti, Cr, Mn, Fe, Co, Ni, Zr, Nb, Ru, Rh, Hf, Ta, Re, Os, Ir, Pt, La, Sn, and Eu; and

(b) a liquid crystal deposited over the surface, the liquid crystal including a moiety that reversibly binds to the metal of the metal complex such that at least a portion of the liquid crystal is bound to the metal complex;

wherein the metal complex is capable of reversibly or irreversibly binding a portion of the compound to be detected, such that when the compound is present in the sample, the portion of the compound will

interact with the metal complex and displace at least some of the liquid crystal that was bound to the metal complex.

As set forth above, independent claim 60 is directed to a device for detecting the presence of a compound in a sample that includes (a) a surface including functional groups and (b) a liquid crystal deposited over the surface. As recited in claim 60, the functional groups are bonded to a metal forming a metal complex. The specification provides significant guidance which Applicants believe is more than adequate to enable a person of skill in the art to prepare the device of claim 60. As set forth in [0013] and [0014] of the specification, the functional group of the device may be a carboxylic acid group on the alkanethiol that is used to form a self-assembled monolayer on the metal surface. [0065] of the specification provides a list of various functional groups that may be used in accordance with the invention. Furthermore, this paragraph specifically teaches that metal carboxylates, a type of metal complex, may be formed by contacting a metal salt with a carboxylic acid. A list of preferred alkanethiols with carboxylic acid functional groups is also set forth in [0065] and includes compounds of formula $\text{HS}(\text{CH}_2)_n\text{CO}_2\text{H}$. A list of preferred metals and specific metal salts for use in preparing the metal complex is also provided in the paragraph [0065]. [0069] of the specification describes specific methods for preparing a surface with carboxylic acid functional groups. As clearly described in [0069], such a surface may be readily formed by contacting an ethanolic solution of an alkanethiol bearing a functional group such as a carboxylic acid with a metallized surface. The alkanethiol bearing the functional group is adsorbed on the metallized surface to provide a surface with carboxylic acid functional groups. The surface bearing the carboxylic acid functional group may then be contacted with a metal salt to form a metal complex such as a metal carboxylate according to the procedure described in [0072]. [0069] and [0072] are set forth below for the Examiner's convenience.

[0069] The concentration of the alkanethiol in the solution used for alkanethiol adsorption generally ranges from about 1 micromolar to 10 millimolar. A preferred concentration range is 100 micromolar to 2 millimolar, with adsorption times ranging from typically 2 minutes to 24 hours. A preferred adsorption time is between 1 hour and 6 hours. Typically, preferred surfaces were prepared by contacting metallized surfaces of a support with an ethanolic solution of an alkanethiol with a functional group such as $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ or a mixture of $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ and $\text{H}_3\text{C}(\text{CH}_2)_{10}\text{SH}$ at a total alkanethiol concentration

of 1 mM for a period of at least about 1 hour. Longer or shorter contact times may be used as long as a densely packed monolayer is obtained as will be apparent to those of skill in the art. Generally, the lower the concentration of the alkanethiol in the alkanethiol solution, the longer the metallized surface will be contacted with the alkanethiol solution. Conversely, the higher the concentration of the alkanethiol in the alkanethiol solution, the longer the metallized surface will be contacted with the alkanethiol.

[0072] A surface presenting functional groups for interacting with a compound to be detected may also be prepared by contacting a metal salt with a first region of a metallized top surface that includes a functional group such as a carboxylic acid to prepare a first region with a metal carboxylate. Other regions of the metallized top surface may then be contacted with salts of other metals or with solutions of different concentrations to provide a device with different sensitivities towards compounds to be detected. For example, a metallized top surface that includes one region with Cu^{+2} carboxylates and another region with carboxylic acids may be prepared such that amines are detected in one area and dialkyl alkylphosphonates are detected in the other regions. The spotting of the metal salts onto various parts of a surface may be done by hand using simple techniques, other techniques for spotting may be used that are known to those skilled in the art. For example, any spotting technology associated with the development of biological microarrays may be employed such as, but not limited to, gene chip spotting machines. This methodology may be extended to provide an array for the detection of multiple types of compound in a sample or to provide a device with differing sensitivities towards the compound.

Applicants believe that the paragraphs described above readily enable a person skilled in the art to construct the device set forth in independent claim 60 and the claims that depend from it. Further enablement, however, is provided in the Examples section of the specification. For example, [0090] describes specific procedures for preparing self-assembled monolayers on an obliquely-deposited gold surface by immersing the gold surface in ethanolic solutions of $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ or a mixture of $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ and $\text{H}_3\text{C}(\text{CH}_2)_{10}\text{SH}$. Therefore, this paragraph specifically teaches how to make a surface that includes functional groups as recited in independent claim 60. [0099] describes the preparation of self-assembled monolayers with metal carboxylate groups. The procedure includes forming a self-assembled monolayer on a gold film using an ethanolic solution of $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ to first produce a surface with carboxylic acid functional groups. The surface is then treated with a solution of a metal salt to form the metal carboxylate metal complex. Therefore, [0099] specifically teaches how to make a surface with functional groups that are bonded to a metal to form a metal complex as recited in claim 60. Those skilled in the art, would readily understand how

to modify the procedures set forth in these paragraph to include different functional groups or different metals such as those recited in claim 60 by simply using different functional groups or different metal salts such as those recited in [0065]. [0065], [0090], and [0099] are set forth below for the Examiner's convenience.

[0065] Various functional groups that interact with the compound to be detected may be used in accordance with the present invention. Examples of such groups include, but are not limited to: acids such as, but not limited to, carboxylic acids, hydroxamic acids, sulfonic acids, sulfinic acids, phosphonic acids, and phosphinic acids; metal complexes of acids such as metal carboxylates or metal sulfonates; nitrogen-containing functional groups such as pyridine, bipyridine, alkylamines, and phenylamines; metal complexes of amines; phosphines; metal complexes of phosphines; metal complexes of acetoacetoxy groups; ketones and aldehydes; and silicon-containing functional groups such as silanols. Preferred functional groups include carboxylic acids and metal carboxylates the latter of which are preferably formed by contacting a metal salt with a carboxylic acid. An especially preferred functional group is a carboxylic acid group on an alkanethiol and metal carboxylates formed therefrom. Preferred alkanethiols with carboxylic acid groups include alkanethiols with the formula $\text{HS}(\text{CH}_2)_n\text{CO}_2\text{H}$ where n is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 or more preferably where n is inclusively from 5 to 18, inclusively from 8 to 12, or where n is 10. Preferred metal carboxylates include those prepared from transition metals such as, but not limited to, Cu, Ag, Au, Zn, Ti, V, Cr, Mn, Fe, Co, Ni, Zr, Nb, Mo, Ru, Rh, Pd, Hf, Ta, W, Re, Os, Ir, and Pt, and other metals such as La, Sn, and Eu. In addition to the above list and Cu^{+2} , preferred metal salts for preparation of metal complex functional groups include Ni^{2+} , Ir^{3+} , Zn^{2+} , Co^{2+} , Mn^{2+} , Fe^{3+} , V^{3+} , Sn^{4+} , La^{3+} , Ag^{1+} , Zr^{4+} , and Eu^{3+} . Copper carboxylates, and particularly Cu^{+2} carboxylates are particularly preferred metal carboxylate functional groups for use in the present invention although one skilled in the art will recognize that choice of the functional group and the moiety of the liquid crystal will depend on the type of compound to be detected.

[0090] Self-assembled monolayers (SAMs) were formed on the surfaces of obliquely deposited films of gold by immersing the films in ethanolic solutions containing either 1 mM $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ or a mixture of $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ and $\text{H}_3\text{C}(\text{CH}_2)_{10}\text{SH}$ (1 mM total thiol concentration) for one hour. The composition of the mixed SAMs formed from $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ and $\text{H}_3\text{C}(\text{CH}_2)_{10}\text{SH}$ were estimated from contact angle measurements (see below). After rinsing in ethanol and drying under nitrogen, the SAMs were immersed for approximately one minute in aqueous solutions adjusted to pH 2.5 (about 1 mM HCl) or pH 3.2 (about 1 mM H_3PO_4). Upon removal from aqueous solution, the surface of a slide was placed under a stream of nitrogen gas to displace excess solution from the surface. Under these conditions, excess salts are not deposited onto the surface. All buffered solutions were used within 12 hours of preparation.

[0099] Self-assembled monolayers (SAMs) were formed on the surfaces of obliquely deposited films of gold by immersing the films in ethanolic solutions containing 1 mM $\text{HOOC}(\text{CH}_2)_{10}\text{SH}$ for one hour. After rinsing in

ethanol and drying under nitrogen, the SAMs were immersed for 5 minutes in ethanolic solutions of $\text{Cu}(\text{ClO}_4)_2$ or $\text{Cd}(\text{NO}_3)_2$. The areal density of the metal was manipulated by controlling the concentration of copper or cadmium in solution between 0.1 μM to 100 mM. Upon removal from the ethanol, the surface of a slide was rinsed with ethanol and then placed under a stream of nitrogen gas to displace excess solution from the surface. All copper and cadmium solutions were used within 6 hours of preparation.

Applicants respectfully contend that those skilled in the art would certainly understand how to prepare a surface with functional groups that are bonded to a metal to form a metal complex such as a metal carboxylate based on the paragraphs described above. For this reason, Applicants respectfully contend that claim 60 and the claims that depend from it are fully supported and enabled by the specification.

Independent claim 67 is set forth below for the Examiner's convenience.

67. (Previously Presented) A device for detecting the presence of a compound in a sample, comprising:

(a) a surface including functional groups, wherein the functional groups are bonded to a first metal in a first region forming a first metal complex and the functional groups are bonded to at least a second different metal in at least a second region of the surface forming at least a second metal complex; and

(b) a liquid crystal deposited over the surface, the liquid crystal including a moiety that reversibly binds to the metal of at least the first metal complex such that at least a portion of the liquid crystal is bound to the first metal complex;

wherein at least the first metal complex is capable of reversibly or irreversibly binding a portion of the compound to be detected, such that when the compound is present in the sample, the portion of the compound will interact with at least the first metal complex and displace at least some of the liquid crystal that was bound to the first metal complex.

Independent claim 67 is also directed to a device for detecting the presence of a compound in a sample that, like independent claim 60, includes (a) a surface with functional groups and (b) a liquid crystal deposited over the surface. In claim 67, the functional groups are bonded to a first metal in a first region forming a first metal complex and the functional groups are bonded to at least a second different metal in at least a second different region of the surface forming at least a second metal complex. Therefore, independent claim 67 includes a surface with functional groups and at least two different regions. One of the regions includes a metal complex formed from one metal, and the second region includes a metal complex formed from a second

metal. The procedures for forming a surface with functional groups is well-described in the specification and is certainly enabled by the specification as described above with respect to independent claim 60. As noted above, with respect to independent claim 60, metal complexes may be readily formed by contacting a surface having a functional group such as a carboxylic acid with a solution that includes a metal salt to form the metal complex. A device with at least two different regions having two different metal complexes may be readily formed by simply contacting two different regions of the surface with solutions that include different metal salts. The different regions may be separately contacted using spotting techniques. This is specifically set forth in [0072] of the specification which is set forth below.

[0072] A surface presenting functional groups for interacting with a compound to be detected may also be prepared by contacting a metal salt with a first region of a metallized top surface that includes a functional group such as a carboxylic acid to prepare a first region with a metal carboxylate. Other regions of the metallized top surface may then be contacted with salts of other metals or with solutions of different concentrations to provide a device with different sensitivities towards compounds to be detected. For example, a metallized top surface that includes one region with Cu^{+2} carboxylates and another region with carboxylic acids may be prepared such that amines are detected in one area and dialkyl alkylphosphonates are detected in the other regions. The spotting of the metal salts onto various parts of a surface may be done by hand using simple techniques, other techniques for spotting may be used that are known to those skilled in the art. For example, any spotting technology associated with the development of biological microarrays may be employed such as, but not limited to, gene chip spotting machines. This methodology may be extended to provide an array for the detection of multiple types of compound in a sample or to provide a device with differing sensitivities towards the compound.

A device with at least two different metal complex regions may also be formed using a fluidic channel to deliver the solution to localized regions of the surface as described in [0074] which is set forth below for the Examiner's convenience.

[0074] Those skilled in the art will recognize that variations on the above procedure could also be used to produce a multiarray. In one such preferred procedure, rather than "spotting" droplets of liquid on a surface, a fluidic channel (e.g., made from micromolded polydimethylsiloxane) is used to deliver liquids to localized regions of a surface similar to the stamping method described above. Generally, any method known to those skilled in the art for delivering liquids to localized regions of a surface could be used to produce the preferred microarray devices for detecting compounds in samples.

Based on the guidance provided in the specification, Applicants respectfully contend that those skilled in the art would be enabled to make and use the device set forth in independent claim 67 and the claims that depend from it. Therefore, for the reasons set forth above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 60, 62-64, and 67-72 under the first paragraph of 35 U.S.C. § 112.

CONCLUSION

In view of the above remarks, it is respectfully submitted that all rejections and objections have been overcome, and that this application is in condition for allowance. Examiner Cole is cordially invited to telephone the undersigned at the number listed below if she believes such would be helpful in advancing the application to issuance.

Respectfully submitted,

Date July 22, 2005

By 

FOLEY & LARDNER LLP
Customer Number: 23524

23524

PATENT TRADEMARK OFFICE
Telephone: (608) 258-4281
Facsimile: (608) 258-4258

Bernard P. Friedrichsen
Attorney for Applicant
Registration No. 44,689